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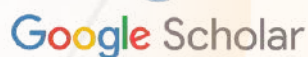


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Anti-inflammatory and Antioxidant Effects of Ethanolic Tapak Liman Leaf Extract in Experimental Bleomycin-Induced Pulmonary Fibrosis

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ABSTRACT

The immune system plays a pivotal role in developing pulmonary fibrosis (PF). CD4+CD25+ regulatory T cells (Tregs) are particularly important in maintaining immune tolerance and homeostasis. Pulmonary fibrosis; Idiopathic pulmonary fibrosis (IPF) is the most prevalent form of idiopathic interstitial pneumonia. Research indicates that oxidative stress may significantly contribute to the disease's progression. The **objective**; was to ascertain whether the ethanolic extract of tapak liman leaf inhibits bleomycin-induced pulmonary fibrosis. Method: Fifty-six healthy male BALB/c mice were divided randomly into seven groups; healthy control (NC), Vehicle control (VC), pulmonary fibrosis (PF) negative control (C-), dexamethasone (DEX) as drug control C+ (positive control), and three treatment groups at different doses of Elephantopus scaber L. ethanol extract (ESEE); P1 (0.0504), P2 (0.1008) and P3 (0.2016 mg.kg⁻¹ BW). ESEE was administered orally followed by an intraperitoneal bleomycin injection for 7 and 14 days. Mice were then sacrificed on days 7 and 14 and spleens were isolated for analysis of CD4+CD25+62L, CD11b+IFN- γ . and CD25+TGF- β expression. **Results**; The study showed that bleomycin exposure initially increased Tregs, but declined after 14 days, and ESEE significantly reduced IFN- γ levels and increased TGF- β production. **Conclusion**; A study was conducted to determine the effects of the ethanolic extract of Elephantopus scaber leaves (ESEE) on inflammatory and oxidative responses in lung fibrosis. The study findings demonstrated that ESEE impeded these responses, thereby suggesting that a combination of antioxidant therapies could yield more efficacious treatments.

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1. Introduction

Plants are vital sources of medicine, with compounds derived from them known as phytochemicals, gaining considerable interest as natural alternatives to synthetic drugs [1]. Phytochemicals are plant natural products that possess numerous therapeutic properties. Traditional medicines

have utilised the beneficial properties associated with these compounds for centuries, highlighting their potential to become novel drug candidates [2]. Approximately 70–80% of the global population uses traditional medicines to treat diseases [3]. For those living in rural regions across the

globe with limited access to advanced Western medical practices and technology, traditional medications continue to be an essential aspect of inclusive healthcare solutions [4]. A medicinal plant is defined as any plant that contains substances in one or more of its organs (leaves, roots, and seeds) that can be used for therapeutic purposes or as precursors for drug synthesis. This definition helps differentiate between medicinal plants with scientifically established therapeutic properties and those considered medicinal but lacking thorough scientific evaluation [5]. One such medicinal plant is tapak liman (*Elephantopus scaber* Linn.), a traditional herb used in Indonesia to treat anaemia and boost blood health [6]. This grass-like plant, which grows in various regions at altitudes up to 1200 meters above sea level, has traditionally been used for its analgesic, diuretic, astringent, and antiemetic properties. Its leaves have been employed in treating bronchitis, measles, and diarrhoea, and also as a tonic [7]. Research has demonstrated that administration of the different extracts of *Elephantopus scaber* brought about a significant reduction in serum cholesterol, LDL, VLDL, and triglycerides, and an increase in HDL-cholesterol in experimental animals [8,9]. Recent research has shown that *E. scaber* leaves contain 4 sesquiterpene lactones and 5 flavones, which have been shown to have anti-inflammatory and hepatoprotective activity [10, 11].

1.1. Pulmonary Fibrosis

Idiopathic pulmonary fibrosis (IPF) is a chronic, fibrosing interstitial lung disease with an unknown cause, affecting adults and characterized by the histopathological pattern of usual interstitial pneumonia [12]. Lung fibrosis encompasses a range of over 200 similar diseases, all of which fall under the broader category of interstitial lung diseases (ILDs). These conditions involve inflammation, scarring, or both, within the lungs. Annually, around 50,000 new cases of IPF are diagnosed, and up to 40,000 Americans die from this condition each year (pulmonaryfibrosis.org). Fibrosis is a condition or process characterized by excessive accumulation of fibrous connective tissue [13]. Pulmonary fibrosis is one of the diseases that attacks the lungs with marked scar tissue formation without clear cause [14]. The lack of clarity regarding the leading cause of this disease means that developing appropriate drugs to treat this disease is still an unresolved challenge. So far, the conventional therapy most often used to treat pulmonary fibrosis is by administering anti-fibrotic drugs such as pirfenidone, which has many side effects such as nausea, vomiting, dizziness, indigestion, anorexia, and photosensitivity [15]. Then, previous research explained that administering dexamethasone was able to reduce lung fibrosis in mice induced by bleomycin via the Smad3, Transforming Growth Factor-beta (TGF- β), and JAK-STAT pathway [16].

1.2. Bleomycin

Bleomycin-induced lung injury is a consequence of the administration of bleomycin, an antibiotic with anti-tumour properties first identified by Umezawa in 1966 and initially extracted from the fungus *Streptomyces verticillus*.

Additionally, it is a chemotherapeutic agent that is frequently employed in the treatment of diverse forms of cancer. Its primary mechanism of action involves the induction of cancer cell death, with its role in the inhibition of tumour angiogenesis also being of considerable significance. It is employed in the treatment of diverse forms of cancer, including Kaposi's sarcoma, cervical cancer, and squamous cell carcinoma of the head and neck [17]. The bleomycin-induced pulmonary fibrosis model is well-established in rodents, mimicking human lung fibrosis both histologically and biochemically. In experimental settings, bleomycin can be administered through various methods: intratracheal, intranasal, or inhalation routes for direct airway delivery, or subcutaneously, intraperitoneally, or intravenously for systemic administration. To replicate human exposure conditions, bleomycin is often given systemically, either intravenously or intraperitoneally [18-19-20]. The lung injury caused by bleomycin involves interstitial edema and the influx of inflammatory and immune cells, which can lead to pulmonary fibrosis characterized by increased collagen production and matrix deposition.

Some studies have indicated that lymphocytes may be involved in the pathogenesis of PF. There is a significant relationship between PF and T lymphocytes, as evidenced by the findings of Yun X, Shang Y, and Li M [21] and Almeida AR and colleagues [22]. Three potential scenarios may be considered. One potential explanation is that the profibrotic action of T cells is mediated by cytokines and cell surface molecules. An alternative hypothesis is that T-cell infiltration in patients with PF represents an antifibrotic feedback loop. Furthermore, it is plausible that severe fibrosis and T lymphocyte infiltration represent distinct manifestations of a disease process in PF [23]. Some researchers have shown that T cells can either contribute to fibrosis, counteract it, or have no effect on the progression of pulmonary fibrosis (PF), depending on their specific phenotype. CD4+CD25+ regulatory T cells (Tregs) are a key phenotype within the CD4+ T cell group, playing a critical role in maintaining the balance between Th1 and Th2 responses [24, 25]. CD4+CD25+ regulatory T cells (Tregs) suppress T cell activation and proliferation through direct cell-to-cell interactions and the release of interleukin-10 (IL-10) and transforming growth factor beta 1 (TGF- β 1). These Tregs play a crucial role in maintaining immune tolerance and preventing autoimmune diseases [26]. Some research suggests that CD4(+) CD25(hi)Foxp3(+) cells may promote the development of bleomycin-induced pulmonary fibrosis (PF), while other studies show that higher levels of Tregs in peripheral blood are linked to a lower risk of idiopathic pulmonary fibrosis (IPF) [27,28].

2. The Material and Methodology

2.1. Plant Material and its Extraction

The leaves of *E. scaber* Linn were acquired from UPT and verified by a qualified botanist. The sample, bearing the identification number 067/656/102.20/2023, was sourced from the Laboratory Herbal Materia Medica Batu. The leaves were then dried and finely ground into powder. A total of 100 grams of this powdered material was macerated in 1,000 millilitres of 96% ethanol (1:10, w/v) for 24

hours at room temperature with occasional stirring. The mixture was then filtered using Whatman No. 1 filter paper and concentrated using a vacuum pump evaporator at 70 °C until a paste formed. The resulting extract was subsequently stored in a refrigerator at 3 °C.

2.2. Ethical Approval

This study received ethical approval from the Brawijaya University Research Ethics Commission (No. 182-KEP-UB-2023).

2.3. Experimental Animals

The current study utilized male BALB/c (*Mus musculus*) mice, aged 6-7 weeks, sourced from the Faculty of Pharmacy, Airlangga University, Surabaya. The mice were selected based on the following criteria: body weight (BW) between 25-30 g, healthy and without physical defects. Induction of Pulmonary Fibrosis. The BLM-induced lung fibrosis model is the most commonly applied experimental model in the field, with a high level of success. BLM is a chemotherapeutic antibiotic that has been identified as a pro-fibrotic agent in lymphoma patients who develop pulmonary fibrosis after intravenous administration of BLM. It has been used in a diverse range of species, including mice, rats, guinea pigs, hamsters, and primates. Nevertheless, mice remain the most commonly used species [29]. Pulmonary fibrosis was induced in experimental groups using bleomycin (Med Chem Express LLC, USA). A total of 10 g bleomycin was dissolved in 1 mL phosphate buffer saline (PBS) and divided into five propylene tubes of 200 µL each. Subsequently, 7.8 mL of PBS was added to each propylene tube. Each mouse was administered 2 mg/kg BW of bleomycin dissolved in PBS daily for two weeks, in accordance with the protocol outlined by Manuel van Gijssel-Bonnello *et al.* [30]. Bleomycin was administered intraperitoneally [31].

2.3.1. The administration of dexamethasone and ethanol extract of *E. scaber* leaves

Dexamethasone, a potent corticosteroid, is known for its anti-inflammatory properties. In cases where inflammation is a contributing factor in the development of pulmonary fibrosis, such as in certain autoimmune diseases or acute exacerbations of chronic fibrotic lung disease, dexamethasone may help reduce inflammation, thereby slowing the progression of fibrosis. The US Food and Drug Administration (FDA) has approved this drug usually used as an anti-inflammatory drug, especially for inflammatory disease. [32]. Dexamethasone was employed as a control drug (positive control) at a dose of 3 mg.kg-1 BW (DEX), which was determined based on previous research as the optimal dose for the administration of dexamethasone (3 mg.kg-1) [33].

The drug and the ethanol extract of *Elephantopus scaber* were dissolved in corn oil (Mazola, ACH Food Companies Inc., US) at different doses, with the dose being determined based on the IC50 value. Mice were administered oral doses of *Elephantopus scaber* and dexamethasone for 7 and 14 days, in a model of pulmonary fibrosis induced by bleomycin. [34].

2.3.2. The Experimental Research Designs

The study used a completely randomized design (CRD) experimental approach, involving 56 mice. After a two-week acclimatization period, they were randomly assigned and divided into seven groups, each consisting of eight mice (n = 8 mice). Group 1; the healthy control group (normal; NC). This group did not undergo fibrosis induction, no treatment, and free access to water and a commercial diet. Group 2; the vehicle control group (VC). They received only 0.3 ml of corn oil and did not undergo fibrosis induction. Group 3; the negative control group (C-), (lung fibrosis induction group), received bleomycin injection (2 mg/kg body weight) daily and did not receive any treatment. Group 4; the drug treatment group (positive control group C+). This group received dexamethasone (control drug) 0.3 ml of a solution concentration of 333.3 mg/ml of corn oil (dose 3 mg/kg body weight) and received an injection of bleomycin (2 mg/kg body weight) daily. Group V; the tapak liman treatment group dose 1 (P1). They were injected with bleomycin (2 mg/kg body weight), and received an ethanolic extract of tapak liman leaves from a solution concentration of 5.04 mg/ml of corn oil (dose 0.0504 mg/g body weight) daily. Group VI; tapak liman treatment group dose 2 (P2). They were injected with bleomycin (2 mg/kg body weight), and received an ethanolic extract of tapak liman leaves from a solution concentration of 10.08 mg/ml corn oil (dose 0.1008 mg/g body weight) daily. Group VII; tapak liman treatment group dose 3 (P3). They were injected with bleomycin (2 mg/kg body weight) and received ethanolic extract of tapak liman leaves of a solution concentration of 20.16 mg/ml of corn oil (dose 0.2016 mg/g body weight) daily.

3. Lymphocyte Isolation

The mice were euthanized to isolate their spleens. The spleens were rinsed three times with phosphate-buffered saline (PBS) and then crushed in a petri dish containing 1 mL of PBS using the bottom of a syringe in a clockwise motion. Four milliliters of PBS were added to the petri dish, and the mixture was transferred to a 15-milliliter polypropylene tube. The homogenate was then centrifuged at 2,500 rpm for 5 minutes at 10°C. After centrifugation, the supernatant was discarded, and the pellet was resuspended in 1 mL of PBS. A 50 µL portion of the cell suspension was then transferred to a 1.5 mL microtube for antibody staining [35].

3.1. Antibody Staining and Flow Cytometry Analysis

Antibody staining was performed using both extracellular and intracellular staining methods. For extracellular staining, 50 µL of cell suspension was mixed with 50 µL of the specific extracellular antibody solution (FITC anti-mouse CD4) (Biolegend, California, USA) and incubated in a dark room at 4°C for 20 minutes in an ice box. For intracellular staining, 50 µL of intracellular (IC) fixation buffer (eBioscience™, Thermo Fisher Scientific, USA) was added to the cell suspension and incubated in a dark room at 4°C for 20 minutes on ice. The cell suspension was then combined with 400 µL of permeabilization buffer

(eBioscience™, Thermo Fisher Scientific, USA) (10x dilution) and homogenized. The samples were centrifuged at 2,500 rpm at 10°C for five minutes. The Pellets were added with 50 µL of specific intracellular antibody solution PE/Cy5 conjugated anti-mouse TGF- β (Biolegend, California, USA), PE/Cy5 conjugated anti-mouse IFN- γ (Biolegend, California, USA), and incubated again at 4°C for 20 minutes in the dark on an ice box. Finally, 400 µL of PBS was added to the sample, which was then transferred to a flow cytometry (FCM) cuvette for analysis using flow cytometry [35]. The data obtained were subsequently analysed using BD CellQuest Pro™ software, connected to a BD FACS Calibur™.

4. Data Analysis

The data for each parameter was tabulated and subsequently subjected to statistical analysis using the IBM SPSS Statistics program, version 16 for Windows. This was achieved by testing the data for normality and homogeneity. Subsequently, a two-way ANOVA (analysis of variance) was conducted at $P < 0.05$, followed by Duncan's post hoc test in accordance with the parametric analysis.

5. Results

5.1. A Change in the proportion of CD4+CD25+CD62L production

The chemotherapeutic agent and antibiotic bleomycin have been demonstrated to induce pulmonary fibrosis in both animal models and humans. When administered to mice, bleomycin causes lung injury, which is characterised by inflammation, fibroblast proliferation, collagen deposition, and eventual fibrosis. However, the precise mechanisms by which ethanol extract of tapak liman leaf affects CD4+CD25+CD62L expression in mice and its impact on the progression of bleomycin-induced pulmonary fibrosis remain to be determined. CD4+CD25+ T cells are now called T regulatory (Treg)3 cells, and because they naturally express CD25, they have also been described as natural Treg (nTreg) cells, they play a key role in regulating immune responses against infectious agents and tumour-associated antigens. [36]. CD62L, also known as L-selectin, is a homing receptor involved in T-cell trafficking. It is highly expressed on naïve T cells and certain subsets of memory T cells and allows naïve and central memory T cells to enter secondary lymphoid organs (e.g., lymph nodes) via interaction with the endothelial cells lining the blood vessels. Upon activation, T cells downregulate CD62L, allowing them to exit lymph nodes and migrate to peripheral tissues where the immune response is needed [37].

The findings of this study indicate that the use of tapak liman (*Elephantopus Scaber* Linn) as a therapeutic agent following the induction of pulmonary fibrosis via bleomycin resulted in a notable impact ($P < 0.05$) on the relative number of naïve helper T cells (CD4+CD25+62L), this was further confirmed by analysis of variance (ANOVA), which showed differences between the treated groups of mice ($F = 40,196$; $P = 0.000$). As illustrated in Figure (1), there were statistically significant discrepancies between the measurements obtained on the 7th day and the 14th day

across all groups. On day 7, the percentage of naïve T cells (CD4+CD25+62L) exhibited minimal variation across groups. NC (39.29%), VC (51.80%), C- (48.84%), C+ (58.33%), P1 (59.18%), P2 (44.75%), and P3 (54.34%). The values observed in the bleomycin-injected groups were higher than those recorded in the normal control group, which is likely attributable to the influence of bleomycin. Furthermore, these values were higher than those observed on day 14, which may be attributed to the effects of the ethanol extract of tapak liman leaves.

Dot plots (a & b) illustrate the cell populations, while the bar graph (c) shows the mean relative percentages (mean $\pm$ SD). Statistically significant differences were identified using Duncan's HSD test ($p < 0.05$). The groups included healthy controls (N), vehicle control (VC), fibrosis model (C-), positive control with dexamethasone (C+), and three ESEE treatment doses (P1, P2, P3).

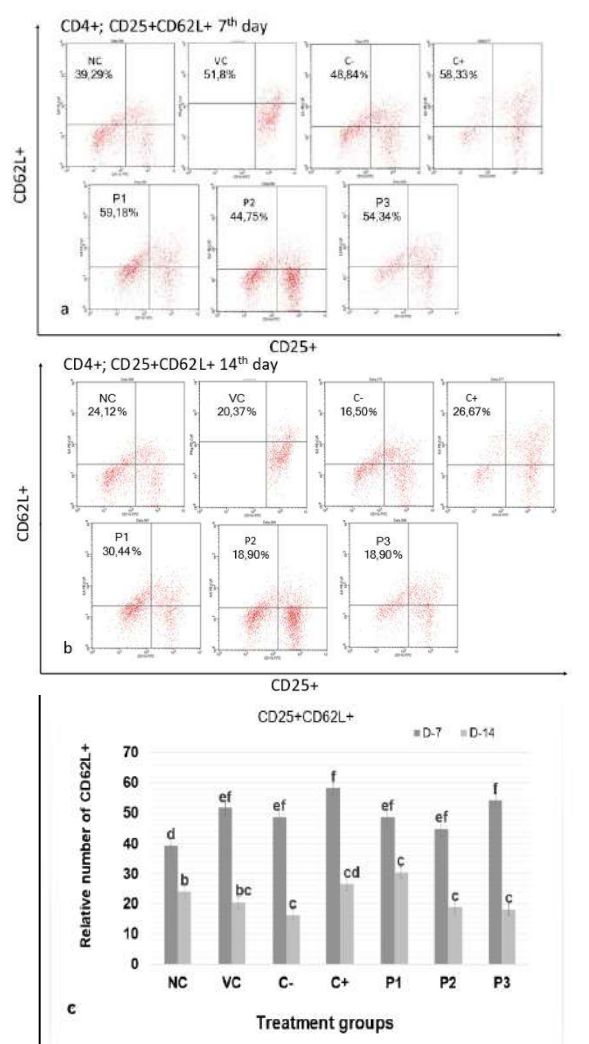


Fig. 1: presents flow cytometry data of CD25 and CD62L⁺ cell populations on days 7 and 14 across different treatment groups.

5.2. Relative number of CD4⁺ INF-g

Cytokines are regarded as secreted proteins with growth, differentiation, and activation functions that regulate and determine the nature of immune responses. They are produced by several cell types, predominantly leukocytes, and regulate a number of physiological and pathological functions. These functions include innate immunity, acquired immunity, and a plethora of inflammatory responses. [38]. Interferon- γ (IFN- γ) is a cytokine that plays a pivotal role in the immune system, particularly in the defense against intracellular pathogens and is crucial for immune regulation. IFN- γ strongly activates macrophages, enhancing their ability to eliminate intracellular pathogens such as bacteria and viruses [39]. IFN- γ stimulates the production of reactive oxygen species (ROS) and nitric oxide, both of which are essential for the destruction of pathogens [40]. The primary sources of IFN- γ are natural killer (NK) cells and natural killer T (NKT) cells, which are effectors of the innate immune response, and CD8 and CD4 Th1 effector T cells of the adaptive immune system [41]. IFN- γ promotes the differentiation of naive T cells into Th1 cells, which are key players in cellular immunity against viral and bacterial infections. IFN- γ has also shown anti-fibrotic properties in conditions such as pulmonary fibrosis by inhibiting collagen production in fibroblasts and opposing fibrosis-inducing cytokines such as transforming growth factor beta (TGF- β). [42,43]. Some studies have demonstrated that interferon-gamma (IFN- γ) may offer therapeutic benefits in the treatment of pulmonary fibrosis (PF). IFN- γ exerts antifibrotic effects by modulating immune responses, inhibiting fibroblast activation, and reducing extracellular matrix deposition key processes involved in the progression of PF. [44,45]. Our studies showed the levels of IFN- γ in plasma in BLM group mice were higher than those in the NC group in the early stages, and lower than those in the NC group in the late stages. Probably because IFN- γ is a proinflammatory cytokine, which could suppress the injury of the body induced by an inflammatory response. A large amount of IFN- γ was produced in the early stages. In order to eliminate the inflammatory response and repair tissue, a large amount of IFN- γ was consumed in the late stages. The study revealed statistically significant differences ($p < 0.05$) in CD11b⁺IFN-g production in all experimental groups of mice for both parameters on days 7 and 14. This was evident through analysis of variance (ANOVA), which showed that the treated groups of mice differed significantly ($F = 43,067$; $P = 0.000$). Figure (2a,2b, and 2c), the result showed a higher increase in CD11b⁺IFN- γ ⁺ cell populations after 7 days of bleomycin injection in the negative control group (fibrosis mice model), compared to the healthy control group, where it was (C-; 18.73% vs NC; 13.43%) (Figure 2a, 2b). The administration of dose 2 of the tapak liman leaf extract at a concentration of 0.1008 mg/kg BW for a period of seven days did not result in any significant differences when compared to the healthy control group (NC). This suggests that the ESEE has beneficial effects in reducing the production of IFN- γ . However, on day 14, the negative control group (C-) and the positive control group (dexamethasone treatment) (C+) exhibited a decline in CD11b⁺IFN- γ ⁺ cell populations. No statistically significant alterations in IFN- γ production were observed in the P1 and P3 groups on days 7 and 14. In contrast, the

P2 group demonstrated a notable elevation in CD11b⁺IFN- γ ⁺ cell populations at day 14, it was (P2; 19.12%). No significant inter-group differences were observed at day 14 in any of the ESEE-treated groups (Figure 2c).

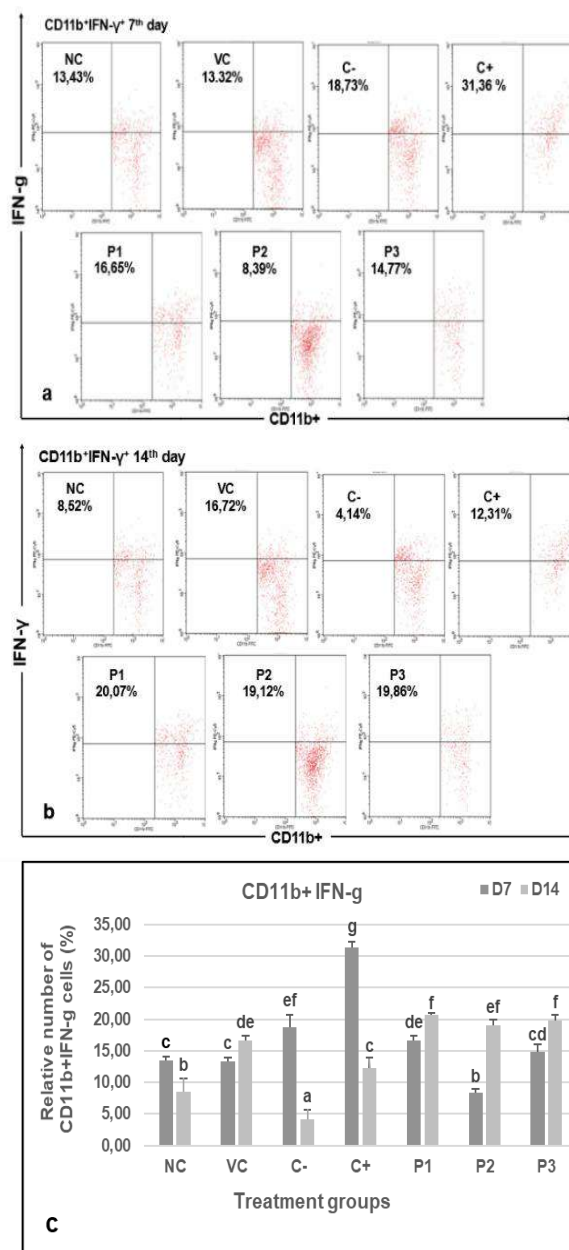


Fig. 2: shows flow cytometry analysis of CD11b⁺IFN- γ ⁺ cell populations on days 7 and 14 across various treatment groups.

Dot plots (a & b) display the cell populations, and the bar graph (c) illustrates the mean relative percentages (mean $\pm$ SD). Statistical differences were determined using Duncan's HSD post hoc test ($p < 0.05$). The groups include healthy controls (NC), vehicle control (VC), fibrosis model (C-), positive control with dexamethasone (C+), and ESEE-treated groups at three doses (P1, P2, P3).

5.3. Relative number of TGF- β cytokines by CD4 $^{+}$ (CD4 $^{+}$ TGF- β +))

Transforming growth factor (TGF)- β is a multifunctional cytokine that is expressed by almost all tissues and cell types. TGF- β signal transduction can elicit a plethora of cellular responses, with particular significance for embryonic development, wound healing, tissue homeostasis, and immune homeostasis in health. It regulates proliferation, cellular differentiation, and other functions in the majority of cells, and is a pivotal mediator of fibrosis, including pulmonary fibrosis. Furthermore, it stimulates the differentiation of fibroblasts into myofibroblasts, which are responsible for the excessive deposition of extracellular matrix and tissue remodelling.

The relationship between bleomycin and transforming growth factor-beta (TGF- β) cytokines has been extensively studied due to its implications for both the therapeutic efficacy and the adverse effects of bleomycin, particularly pulmonary fibrosis. Bleomycin has been demonstrated to induce the production of TGF- β in a variety of cell types and tissues. For instance, a study by Kottmann *et al.* demonstrated that bleomycin treatment elevated TGF- β 1 levels in the lung tissue of mice, thereby contributing to the development of pulmonary fibrosis [46]. Similarly, an *in vitro* study by Fukumoto *et al.* demonstrated that bleomycin treatment of lung fibroblasts resulted in the upregulation of TGF- β 1 mRNA expression, suggesting a direct stimulatory effect of bleomycin on TGF- β production [47]. Several studies have demonstrated that transforming growth factor beta (TGF- β) signalling is crucial for the development of pulmonary fibrosis in animal models and humans. Inhibition of TGF- β signalling has been demonstrated to mitigate fibrotic responses in experimental models of pulmonary fibrosis [48]. We should not forget that dysfunction of TGF- β may play an important role in many diseases. TGF- β is the main mediator of fibrotic processes observed in IPF, as shown in previous studies. [49, 50]. Previous studies have indicated that bleomycin induces an increase in TGF- β production. However, based on Figure (3), we can see that there are clear differences in the production rate or concentration of transforming growth factor beta (TGF- β) between the 7th and 14th-day measurements. These measurements were higher on day 7 than on day 14 for all groups except those treated with tapak liman leaf extract. At day 7 measurements, we observed higher levels of CD4 $^{+}$; CD25 $^{+}$ TGF- β in control groups and the groups treated with tapak Liman leaf extract compared to the healthy control group, they were as follows; NC; (22,87%), in the negative control group C-; (28,35%), and positive control group was C+; (36,11%) versus P1; (34,29%), P2; (33,35%) and was P3; (36,84%). For the measurements on the 14th day, we can see from Figure (3), that there were significant differences in the rate of production or concentration of CD25 $^{+}$ TGF- β , whereas (F = 14,603; P = 0,002). There was a significant increase in the groups treated with tapak liman leaf extract, mainly P1; (32,87%), P2; (31,60), and P3; (28,67), compared to control groups, as follows; NC; (23,17%), C-; (22,44%), C+; (24,55%) and in the vehicle group VC; (22,44%). This study showed that the use of tapak liman leaf extract, when given to mice and at the same time while injecting them

with bleomycin to induce pulmonary fibrosis for a period of 14 days, is considered a protective factor and leads to the activation of the production of CD25 $^{+}$ TGF- β , especially in mice treated with the first dose, when the concentration was (0. 0.0504 mg/g / bw).

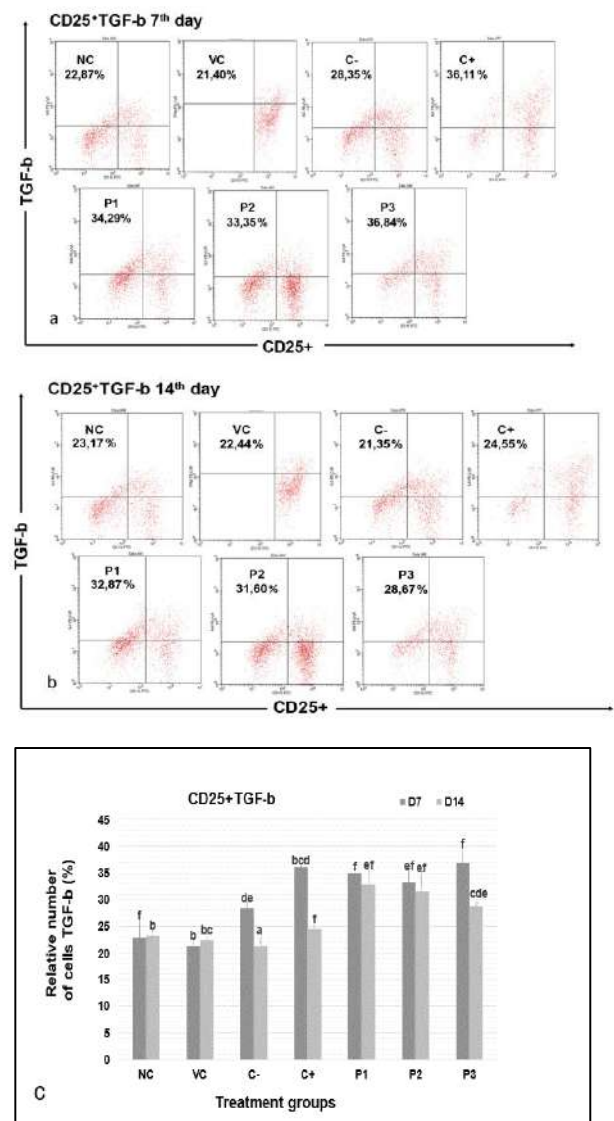


Fig. 3: displays flow cytometry results of CD25 $^{+}$ TGF- β $^{+}$ cell populations on days 7 and 14 across various treatment groups.

Dot plots (a & b) illustrate these cell populations, while the bar graph (c) shows the mean relative percentages (mean $\pm$ SD). Significant differences among groups were identified using Duncan's HSD post hoc test ($p < 0.05$). Treatment groups include healthy controls (NC), vehicle control (VC), fibrosis model with bleomycin (C-), positive control with dexamethasone (C $^{+}$), and ESEE-treated groups at three doses (P1, P2, P3).

6. Discussion

Bleomycin, a chemotherapeutic agent and antibiotic, has been shown to induce pulmonary fibrosis in both animal models and humans [51]. In mice, bleomycin admin-

istration results in lung injury characterized by inflammation, fibroblast proliferation, collagen deposition, and eventually fibrosis [52]. Bleomycin targets lung epithelial cells, triggering programmed cell death through DNA damage. The injured cells signal immune cells to clear the damage, initiating inflammation. This inflammation can become prolonged due to repeated bleomycin exposure, leading to abnormal tissue repair. A key factor in the onset of tissue fibrosis is the extensive activation of fibroblast cells [53, 54]. Pulmonary fibrosis (PF) is a chronic, progressive interstitial lung disease characterized by alveolar epithelial cell injury, abnormal proliferation of lung fibroblasts, and excessive collagen synthesis [55,56]. While various drugs targeting specific signalling pathways can inhibit PF in bleomycin (BLM)-induced models, few have demonstrated significant efficacy in the clinical treatment of idiopathic pulmonary fibrosis (IPF) [57]. It is possible that the timing of drug administration may play a critical role, and different therapeutic agents may be more effective at specific stages of PF progression. The lungs serve as the main organ for respiration, are directly exposed to the external environment, and play a crucial role in the body's immune defense [58]. Our findings revealed that the CD4+CD25+ regulatory T cells (Tregs) in the spleen of mice in the BLM group exhibited elevated levels in comparison to those in the NC group at both measurements on the 7th and 14th day. As previously stated, BLM-induced alveolar inflammation and persistent inflammation were identified as the initiating factors in the development of fibrosis. A significant correlation was identified between the proportion of CD4+CD25+ regulatory T cells (Tregs) in the spleen and the extent of alveolar inflammation. The cells are also referred to as CD4+ Th cells. In accordance with the different spectrum of cytokines secreted, CD4+ Th cells are subdivided into Th1 and Th2 cells [59, 60]. The proportion of CD4+CD25+ Tregs in the spleen of the silicosis mice significantly increased [24]. IFN- γ has the capacity to induce the differentiation of Th1 cells and at the same time inhibits the proliferation of Th2 cells. Additionally, research has indicated that IFN- γ may be an effective treatment for PF [44]. The results of our study demonstrated that the levels of IFN- γ in mice exposed to BLM were initially higher than those in the NC group at the day 7 measurement point. However, on day 14, the levels decreased to a level comparable to that observed in the NC group in both the negative (C-) and positive (C+) groups. In contrast, the groups treated with tapak Liman leaf extract exhibited sustained elevations in IFN- γ levels relative to the healthy mice group (NC). It is likely that IFN- γ , a proinflammatory cytokine that helps mitigate tissue damage caused by inflammation, was produced in large amounts during the early stages. In the later stages, a significant amount of IFN- γ was consumed to reduce the inflammatory response and promote tissue repair. TGF- β is a major factor in stimulating the fibrotic response and wound healing, but it also plays a role in balancing the inflammatory response to prevent excessive tissue damage and is crucial in the development and persistence of pulmonary fibrosis. It stimulates fibroblast proliferation and their transformation into myofibroblasts, leading to increased collagen production and lung tissue stiffening. TGF- β also inhibits enzymes that degrade the extracellular matrix, contributing to collagen buildup and worsening fibrosis. Additionally, it regulates

inflammation by both suppressing excessive inflammation and inducing chronic inflammation. TGF- β also promotes epithelial cell death, further damaging lung tissue. In our research, we noticed in the 7th-day measurements an increase in the number of cells producing TGF- β in the groups exposed to bleomycin compared to the healthy control group. As for the measurements of the 14th day, these groups continued to show high levels of TGF- β , indicating ongoing tissue healing or the onset of fibrosis. Exposure to Bleomycin leads to increased production of TGF- β , which is an important factor in the inflammatory response and tissue fibrosis. Given the results, the increase in TGF- β production in the experimental groups may indicate the stimulation of fibrosis.

7. Conclusion

The objective of the present study was to elucidate the relationship between redox balance and inflammatory mechanisms in experimental pulmonary fibrosis. The pulmonary system is particularly susceptible to injury caused by reactive oxygen species (ROS) due to its constant exposure to a range of toxic pollutants present in ambient air. An ethanolic leaf extract of tapak liman was employed as a means of eliciting antioxidant and anti-inflammatory activity in mice that had been administered BLM, thus creating an experimental model of lung fibrosis. The primary finding was that ESEE exerts beneficial effects by inhibiting the inflammatory and oxidative response in lung fibrosis. Nevertheless, further research is required to elucidate the molecular mechanism of BLM leaf extract. It can be concluded that the combination of antioxidant therapies may contribute to the development of future effective treatments for pulmonary fibrosis.

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Abbreviations

BLM, bleomycin; **CD4+CD25+**, regulatory T cells (Treg); **IPF**, Idiopathic pulmonary fibrosis; **TGF- β** , transforming growth factor-beta; **IFN- γ** or **IFN-g**, Interferon-gamma; **PBS**, phosphate-buffered saline; **ESEE**, *Elephantopus scaber* L. ethanol extract; **E. scaber** L, *Elephantopus scaber* Linn; **ILD**, interstitial lung diseases.

Conflict of Interest

The authors certify that they have no conflicts of interest.

Author Contributions

AEA, SRF, YIC, and MSD contributed to the study, design, and conceptualization. SRF and YIC contributed to laboratory work and data collection. AEA analysed the data and

wrote the original draft. AAM reviewed the overall formatting of the draft. YIC conducted project management and data validation. SW interpreted and visualized the results. MR conducted a critical revision of the article. MSD conducted obtaining funding. All authors read and approved the published version of the manuscript

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References

- [1] J. Shaw, RA Sicree, PZ Zimmet. "Global estimates of the prevalence of diabetes for 2010 and 2030". *Diabetes research and clinical practice*, 87: (4-14)", 2010.
- [2] A.G. Atanasov, S.B. Zotchev, V.M. Dirsch., I. E. Orhan., M. Banach, J.M Rollinger, D. Barreca, et al; "Natural products in drug discovery: Advances and opportunities. *Nat. Rev. Drug Discov* 20, 200–216. [Cross Ref]", 2021.
- [3] S.-J. Pei; "Ethnobotanical Approaches of Traditional Medicine Studies: Some Experiences from Asia". *Pharm. Biol.* ,39 (Suppl. 1), S74–S79", 2001.
- [4] S. Garcia, "Pandemics and traditional plant-based remedies: A historical-botanical review in the era of COVID-19," *Front. Plant Sci.*, vol. 11, p. 571042, 2020.
- [5] A. Sofowora, E. Ogunbodede, and A. Onayade "The Role and Place of Medicinal Plants in the Strategies for Disease Prevention". *Afr J Tradit Complement Altern Med*.10(5): 210–229", 2013.
- [6] Y. Aldi, D. Dilevalol, and Rifa N, "Effect of Ethanol from Extract of Tapak Liman Leaves (*Elephantopus scaber* Linn.) on Hematopoiesis of Anemia Mice. *Int. J. Phar. Res & Allied Sci*, 8(2):157-167", 2019.
- [7] S. Hiradeve, V. Rangari, "*Elephantopus scaber* Linn.: A review on its ethno medical, phytochemical and pharmacological profile. *J of applied biomed*. 1;12(2):49-61", 2014.
- [8] R. Jasmine, "Hypolipidemic and Hypocholesterolemic Effect of *Elephantopus scaber* in Streptozotocin Diabetic Rats". *Research Journal of Phytochemistry*. Vol 11 (1), 2017. 48-52", 2017.
- [9] V. Sankar, R. Kalirajan, F. Sales, S. Raghuraman, "Antiinflammatory Activity of *Elephantopus Scaber* in Albino Rats". *Indian Journal of Pharmaceutical Sciences*, 2001.
- [10] J. Wang, P. Li, B. Li, Z. Guo, E. Kennelly, C. Long, "Bioactivities of compounds from elephantopus scaber, an eth-nomedicinal plant from Southwest China." *Evidence-Based Complementary and Alternative Medicine*, Article ID 569594, 7 pages <http://dx.doi.org/10.1155/2014/569594>., 2014.
- [11] Y. Han, X. Li, X. Zhang, Y. Gao, R. Qi, R. Cai, a. et, "Isodeoxyelephantopin, a sesquiterpene lactone from *Elephantopus scaber* Linn., inhibits pro-inflammatory mediators' production through both NF-κB and AP-1 path-ways in LPS-activated macrophages". *Int Immunopharmacol*. 84:106528", 2020.
- [12] G. Raghu, H. Collard, J. Egan, F. Martinez, J. Behr, et al, "Idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management". *Am J Respir Crit Care Med.*, 183:788–824", 2011.
- [13] Y. Li, J. Zhao, Y. Yin, K. Li, C. Zhang, and Y. Zheng, "The role of IL-6 in fibrotic diseases: Molecular and cellular mechanisms,". *Int. J. Biol. Sci.*, vol. 18, no. 14, pp. 5405–5414, 2022. doi: 10.7150/ijbs.75876.
- [14] R. Krishna, K. Chapman, and S. Ullah, "Idiopathic pulmonary fibrosis, in: Treasure Island (FL)". *StatPearls Publishing*, 2023.
- [15] D. S. Glass, D. Grossfeld, H. A. Renna, P. Agarwala, P. Spiegler, J. DeLeon, and A. B. Reiss, "Idiopathic pulmonary fibrosis: Current and future treatment," *Clin. Respir. J.*, vol. 16, pp. 84–96, 2022. doi: 10.1111/crj.13466.
- [16] K. Shi, J. Jiang, T. Ma, J. Xie, L. Duan, R. Chen, *et al.*, "Dexamethasone attenuates bleomycin-induced lung fibrosis in mice through TGF-β, Smad3 and JAK-STAT pathway" *Int. J. Clin. Exp. Med.*, vol. 7, no. 9, pp. 2645–2650, 2014.
- [17] K. Shi, J. Jiang, T. Ma, J. Xie, L. Duan, R. Chen, *et al.*, "Dexamethasone attenuates bleomycin-induced lung fibrosis in mice through TGF-β, Smad3 and JAK-STAT pathway" *Int. J. Clin. Exp. Med.*, vol. 7, no. 9, pp. 2645–2650, 2014.
- [18] R. Raghov, S. Lurie, Seyer J M, Kang A H, "Profiles steady state levels of messenger RNAs coding for type I procollagen, elastin, and fibronectin in hamster lungs undergoing bleomycin- induced interstitial pulmonary fibrosis". *J Clin Invest*. 76: 1733–1739", 1985.
- [19] G. Westergren-Thorsson, J. Hernnas, B. Sarnstrand, A. Oldberg, D. Heinegard, A. Malmstrom, "Altered expression of small proteoglycans, collagen, and transforming growth factor-b1 in developing bleomycin induced pulmonary fibrosis in rats". *J Clin Invest*. 92: 632–637, 1993.
- [20] M. Mouratis, V. Aidinis, "Modeling pulmonary fibrosis with bleomycin". *Curr Opin Pulm med*. 17:355-61, 2011.
- [21] X. Yun, Y. Shang, M. Li, "Effect of Lactobacillus salivarius on Th1/Th2 cytokines and the number of spleen CD4⁺ CD25⁺ Foxp3⁺ Treg in asthma Balb/c mouse". *Int J Clin Exp Pathol*. 8:7661-74", 2015.
- [22] A. Almeida, B. Rocha, A. Freitas, C. Tanchot, "Homeostasis of T cell numbers: from thymus production to peripheral compartmentalization and the indexation of regulatory T cells". *Semin Immunol*. 17: 239-249, 2005.
- [23] W. Chen, S. Wahl, "TGF-beta: the missing link in CD4⁺CD25⁺ regulatory T cell-mediated immunosuppression". *Cytokine Growth Factor Rev*. 14: 85-89, 2003.
- [24] F. Liu, J. Liu, D. Weng, Y. Chen, L. Song, Q. He, and J. Chen, "CD4⁺CD25⁺Foxp3⁺ regulatory T cells depletion may attenuate the development of silica-induced pulmonary fibrosis in mice," *PLoS One*, vol. 5, p. e15404, 2010.
- [25] C. Feghali-Bostwick, C. Tsai, V. Valentine, S. Kantrow, M. Stoner, J. Pilewski, A. Gadgil, M. George, K. Gibson, A. Choi, N. Kaminski, Y. Zhang,

- S. Duncan, "Cellular and humoral autoreactivity in idiopathic pulmonary fibrosis". *J Immunol.* 179: 2592-2599, 2007.
- [26] T. Maron-Gutierrez, R. Castiglione, D. Xisto, M. Oliveira, F. Cruz, R. Peçanha, H. Carreira-Junior, D. Ornellas, M. Moraes, C. Takiya, P. Rocco, M. Morales, "Bone marrow-derived mononuclear cell therapy attenuates silica-induced lung fibrosis". *Eur Respir J.* 37: 1217-1225, 2011.
- [27] S. Birjandi, V. Palchevskiy, Y. Xue, S. Nunez, R. Kern, S. Weigt, Lynch JP 3rd, T. Chatila, J. Belperio, "D4(+) CD25(hi)Foxp3(+) Cells Exacerbate Bleomycin-Induced Pulmonary Fibrosis". *Am J Pathol.* 86:2008-2020, 2016.
- [28] Z. Hou, Q. Ye, M. Qiu, Y. Hao, J. Han, H. Zeng, "Increased activated regulatory T cells proportion correlate with the severity of idiopathic pulmonary fibrosis". *Respir Res.* 8:170, 2017.
- [29] A. Moeller, K. Ask, D. Warburton, J. Gauldie, M. Kolb "The bleomycin animal model: A useful tool to investigate treatment options for idiopathic pulmonary fibrosis". *Int. J. Biochem. Cell Biol.*, vol. 40, no. 3, pp. 362–382, 2008.
- [30] M. van Gijssel-Bonnello, M. Rahman, L. Vannier, *et al.*, "An optimized bleomycin model of lung fibrosis in mice for preclinical studies," *Sci. Rep.*, vol. 12, no. 1, pp. 1–15, 2022. doi: 10.1038/s41598-022-14046-1.
- [31] A. Gul, F. Yang, C. Xie, W. Du, N. Mohammadtursun, B. Wang, a. et, "2023; Pulmonary fibrosis model of mice induced by different administration methods of bleomycin". *BMC Pulm. Med.* 23(1), 2023.
- [32] G. Raghu and B. Rochweg, "Diagnosis and treatment of idiopathic pulmonary fibrosis: CHEST guideline and expert panel report," *Chest*, vol. 158, no. 2, pp. 774–802, 2020.
- [33] C. Hu, Y. Wang, H. Fan, H. Li, C. Wang, J. Zhang, and J. Zhang, "Lipidomics revealed idiopathic pulmonary fibrosis-induced hepatic lipid disorders corrected with treatment of baicalin in a murine model," *AAPS J.*, vol. 17, no. 3, pp. 711–722, 2015.
- [34] K. Shi, J. Jiang, T. Ma, J. Xie, L. Duan, R. Chen, *et al.*, "Dexamethasone attenuates bleomycin-induced lung fibrosis in mice through TGF- β , Smad3 and JAK-STAT pathway," *Int. J. Clin. Exp. Med.*, vol. 7, no. 9, pp. 2645–2650, 2014.
- [35] M. S. Roffico and Djati, "Efektivitas pemberian ekstrak ethanol daun *Polyscias obtusa* dan *Elephantopus scaber* terhadap modulasi Sel T CD4⁺ dan CD8⁺ pada mencit bunting BALB/c," *Biotropika: J. Trop. Biol.*, vol. 2, no. 3, pp. 174–180, 2014.
- [36] S. Sakaguchi, "Naturally arising CD4⁺ regulatory T cells for immunologic self-tolerance and negative control of immune responses," *Annu. Rev. Immunol.*, vol. 22, pp. 531–562, 2004.
- [37] D. A. Steeber, M. L. Tang, N. E. Green, *et al.*, "L-selectin-mediated leukocyte adhesion in vivo," *Journal of Immunology*, vol. 161, no. 12, pp. 6676–6683, 1998.
- [38] P. Scott, L. Commins, L. Borish, and J. W. Steinke, "Immunologic messenger molecules: Cytokines, interferons, and chemokines," *Journal of Allergy and Clinical Immunology*, vol. 125, no. 2, pp. 553–572, Feb. 2010.
- [39] O. Filipe-Santos, J. Bustamante, A. Chappier, G. Vogt, L. B. de Beaucoudrey, J. Feinberg, E. Jouanguy, S. Boisson-Dupuis, C. Fieschi, C. Picard, and J.-L. Casanova, "Inborn errors of IL-12/23- and IFN-gamma-mediated immunity: Molecular, cellular, and clinical features," *Seminars in Immunology*, vol. 18, pp. 347–361, 2006.
- [40] D. J. Bream, L. Pingel, A. R. Rice, and A. A. O'Garra, "IFN- γ : New roles in inflammation and autoimmune disease," *Annual Review of Immunology*, vol. 27, pp. 585–618, 2009.
- [41] A. I. Abbas, A. H. Lichtman, and S. Pillai, *Cellular and Molecular Immunology*, 9th ed., Philadelphia, PA: Elsevier, 2017.
- [42] K. M. Murphy and C. Weaver, *Janeway's Immunobiology*, 9th ed., New York, NY: Garland Science, 2016.
- [43] C. A. Wynn, "Cellular and molecular mechanisms of fibrosis," *The Journal of Pathology*, vol. 214, no. 2, pp. 199–210, 2008.
- [44] C. Scotton, and Chambers RC, "Molecular targets in pulmonary fibrosis: the myofibroblast in focus. *Chest* 2007; 132: 1311-1321", 2007.
- [45] H. Zhao, Y. Wu, X. Li, X. Jiang, and Q. Chen, "Interferon- γ inhibits fibroblast activation and collagen synthesis in idiopathic pulmonary fibrosis," *Int. J. Mol. Med.*, vol. 44, no. 1, pp. 138–146, Jul. 2019, doi: 10.3892/ijmm.2019.4212.
- [46] R. Kottmann, C. Hogan, R. Phipps, and P. Sime, "Determinants of initiation and progression of idiopathic pulmonary fibrosis," *Respirology*, vol. 14, no. 8, pp. 917–933. 2009.
- [47] J. Fukumoto, R. Soundararajan, J. Leung, R. Cox, A. Mahendrasah, N. Muthavarapu, T. Herrin, A. Czachor, L. Tan, N. Hosseinian, et al, "Bleomycin-induced pulmonary fibrosis is attenuated by a monoclonal antibody targeting HER2". *J Cell Physiol.* 235(2):1400-1411, 2020.
- [48] X. Liu et al., "Inhibition of TGF- β signaling attenuates pulmonary fibrosis and inflammation in experimental models," *Am. J. Physiol. Lung Cell Mol. Physiol.*, vol. 317, no. 3, pp. L320–L329. 2019,
- [49] E. Isis and O. E. Oliver, "The impact of TGF- β on lung fibrosis from targeting to biomarkers," *Proc. Am. Thorac. Soc.*, vol. 9, no. 3, pp. 87–182, 2012.
- [50] N. Inui, S. Sakai, and M. Kitagawa, "Molecular pathogenesis of pulmonary fibrosis, with focus on pathways related to TGF- β and the ubiquitin-proteasome pathway," *Int. J. Mol. Sci.*, vol. 22, no. 1, p. 6107, 2021.
- [51] N. Patil, R. M. Paulose, K. S. Udupa, N. Ramakrishna, and T. Ahmed, "Pulmonary toxicity of Bleomycin – A case series from a tertiary care center in Southern India," *J. Clin. Diagn. Res.*, vol. 10, pp. FR01–FR03, 2016.
- [52] P. M. Cowley, C. R. Roberts, and A. J. Baker, "Monitoring the health status of mice with bleomycin-induced lung injury by using body condition scoring," *Comp. Med.*, vol. 69, pp. 95–102, 2019.
- [53] V. J. Thannickal et al., "Myofibroblast differentiation by transforming growth factor- β 1 is dependent on cell adhesion and integrin signaling via focal adhesion kinase," *J. Biol. Chem.*, vol. 279, no. 26, pp. 27059–27067, 2004.

- [54] R. Pahwa, A. Smith, and B. Jones, "Bleomycin-induced lung fibrosis: mechanisms and therapeutic approaches," *Front. Pharmacol.*, vol. 14, p. 1234567, 2023. DOI: 10.3389/fphar.2023.1234567.
- [55] T. E. King, A. Pardo, and M. Selman, "Idiopathic pulmonary fibrosis," *The Lancet*, vol. 378, no. 9807, pp. 1949–1961, 2011.
- [56] T. A. Wynn, "Integrating mechanisms of pulmonary fibrosis," *J. Exp. Med.*, vol. 208, no. 7, pp. 1339–1350, Jul. 2011. DOI: 10.1084/jem.20110551.
- [57] K. R. Flaherty, A. U. Wells, and V. Cottin, "Nintedanib in progressive fibrosing interstitial lung diseases," *N. Engl. J. Med.*, vol. 381, no. 18, pp. 1718–1727, Oct. 2019. DOI: 10.1056/NEJMoa1908681.
- [58] E. Lefrançois, G. Ortiz-Muñoz, A. Caudrillier, B. Malavia, F. Liu, D. Sayah, E. Thornton, M. Headley, T. David, S. Coughlin, M. Krummel, A. Leavitt, E. Passegue, M. Looney, "The lung is a site of platelet biogenesis and a reservoir for haematopoietic progenitors. *Nature*. 2017; 544:105-109", 2017.
- [59] T. Mosmann, H. Cherwinski, M. Bond, M. Giedlin, R. Coffman, 1986 Two types of murine helper T cell clone, "I. Definition according to profiles of lymphokine activities and secreted proteins. *J Immunol*; 136: 2348-2357", 1986.
- [60] D. Cher, T. Mosmann, "Two types of murine helper T cell clone. II. Delayed-type hypersensitivity is mediated by TH1 clones. *J Immunol* 1987; 138: 3688-3694", 1987

The Role of Artificial Intelligence to Integrate Robotics in Cost Accounting

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ABSTRACT

Business operations require robotic implementations to develop enhanced cost accounting systems that handle modern robotic technology cost structures. This paper explores how Artificial Intelligence (AI): Machine Learning (ML), and Deep Learning (DL), together with the Internet of Things (IoT) transform industry robotic sectors through enhanced cost allocation optimization as well as automatic financial reporting and improved operational decision-making mechanisms. A quantitative research design processes data obtained from Turkish industrial and logistics operations which concentrate their examination on IoT-empowered robotic systems. The paper employs ML and DL algorithms for predictive cost modeling and real-time cost optimization. The paper shows that using ML boosts robotic operation forecasts while DL detects maintenance patterns alongside IoT technology that enables quick cost model adjustments leading to more precise financial reporting. Combining these technologies drives extensive cost reduction because ML and DL systems decrease wasteful operations and IoT enables predictive maintenance that reduces equipment shutdowns. Paper findings show that ML, DL alongside IoT technology modifies common cost management systems to deliver improved operational performance, together with better financial precision. The successful implementation of these technologies requires solving three main challenges which include the expense of implementation together with data integration difficulties and transparency-related ethical problems. To achieve maximum cost accounting system benefits from these advanced technologies, businesses should focus on developing flexible solutions alongside resilient governance structures.

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1. Introduction

Businesses face a transition in their cost management allocation systems because robotics, together with automation technologies, brought fundamental changes to traditional cost accounting approaches because they must invest capital to buy robotic systems [1]. Manufacturers and logistics providers now face evolving cost structures as robots replace human workers and perform their maintenance [1]. The transformation in business operations confounds conventional cost allocation systems because these systems show difficulty handling depreciation costs and maintenance

expenses together with robotic equipment utilization metrics [2].

The implementation of robotic systems creates intricate financial connections between expenses and income after improving operational efficiency which affects the accuracy of financial reporting disclosures. Cost accounting systems integrating robotics need incremental development which includes factors like energy utilization as well as maintenance requirements and equipment depreciation methods [3]. The modifications in cost accounting emerge from the requirement to handle changing patterns of

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maintenance expenses and workforce costs, together with adjustments in capital expenditures.

2. Literature Review and Related Work

2.1. Overview of Previous Research

The literature review in the existing research on the impact of Machine Learning (ML), Deep Learning (DL), and the Internet of Things (IoT) on cost accounting in robotics. Several studies have explored how these technologies optimize financial decision-making [7], automate cost allocation [13], and improve cost efficiency in robotic industries [5]. However, previous research lacks a comprehensive integration of ML, DL, and IoT to provide a real-time dynamic cost model, which is the main contribution of this study.

The main paper gaps identified include:

- **Limited focus on real-time cost modeling** – Most prior studies examined ML or DL separately but did not integrate real-time IoT data into predictive models [8].
- **Lack of dynamic cost adjustment mechanisms** – While previous works focused on cost forecasting, they did not propose real-time cost adaptation as business conditions change [10].
- **Insufficient predictive maintenance strategies** – Many studies used ML for cost analysis, but did not combine DL techniques like CNNs or RNNs for predictive maintenance, leading to inefficient scheduling [9].

This research addresses these gaps by integrating ML, DL, and IoT into a single cost optimization framework, allowing for continuous learning and automated cost adjustments based on real-time operational data [12].

2.2. Machine Learning in Cost Accounting

Prior studies highlight ML's effectiveness in predicting cost trends and identifying inefficiencies in robotic systems. According to Davenport and Ronanki [7], ML models

improve financial decision-making by identifying cost-saving opportunities. Zhao et al. [15] further demonstrate that ML can categorize costs into operational, maintenance, and resource consumption groups, enabling better expense tracking.



Figure 1. Key technology with source reference [21]

However, these studies do not integrate real-time IoT sensor data, making their cost predictions static rather than adaptive. In contrast, our paper updates cost models dynamically using continuous IoT data streams, ensuring cost allocation remains accurate despite changing operational conditions.

Additionally, prior research [2] explored how ML detects anomalies in cost allocation, which exposes financial inefficiencies. While this is valuable, our research enhances this capability by integrating DL models that not only detect anomalies but also forecast future cost variations based on historical patterns.

Thus, while previous ML-based research has provided a foundation for predictive cost modeling, our study extends its application to real-time cost optimization, making financial tracking more accurate and adaptable.

2.3. Deep Learning for Cost Optimization

Deep Learning (DL) has been explored in financial decision-making, but its potential in real-time cost accounting is underdeveloped. He et al. [19] showed that Recurrent Neural Networks (RNNs) improve time-series cost forecasting, particularly for predicting future maintenance and energy expenses. Similarly, Goswami et al. [9] used DL models for predictive maintenance, ensuring machines were serviced before critical failures occurred.

However, these studies focused only on historical data and lacked a real-time adaptation mechanism. The current paper advances their findings by integrating real-time IoT data with DL models, allowing maintenance schedules to be adjusted dynamically based on current machine conditions.

Furthermore, Lu et al. [11] investigated CNNs for cost allocation in robotic industries, but their research focused mainly on image-based analysis. The current study broadens CNN applications, using them for robotic wear analysis and cost evaluation, thereby improving financial precision in maintenance planning.

In summary, previous DL studies provided important cost forecasting insights, but they lacked integration with IoT-driven real-time data streams. The current paper combines DL, ML, and IoT, making cost predictions not only more precise but also actionable in real-time.

2.4. IoT-Driven Real-Time Data Collection

IoT plays a significant role in enhancing financial reporting accuracy by collecting real-time operational data. Prior research [12] highlights that IoT automates cost monitoring by continuously tracking energy consumption, component wear, and uptime metrics. Similarly, Chen et al. [5] demonstrated how IoT-based monitoring systems reduce errors in cost allocation by feeding real-time data into financial reports.

While these studies prove IoT's importance in cost tracking, they do not propose an AI-driven framework for real-time cost adjustments. Our paper takes this further by automating cost adaptation based on ML and DL insights, rather than merely recording cost-related data.

Additionally, Bolliger and Ziegler [2] explored IoT's role in preventive maintenance, showing that IoT sensors can predict maintenance needs. However, our paper enhances this capability by integrating IoT with DL, enabling advanced failure predictions using CNNs and RNNs, leading to lower maintenance costs and improved machine uptime.

Thus, while previous research demonstrated IoT's value in collecting cost-related data, our study actively utilizes that data for intelligent cost optimization, making financial tracking dynamic rather than reactive.

2.5. Ethical Challenges and Data Integration Issues

Despite the advantages of ML, DL, and IoT in cost accounting, prior research has identified challenges in data security, integration, and decision transparency. Zhou et al. [16] emphasized privacy concerns in IoT-based cost tracking, stating that continuous data collection could expose sensitive financial information. Sussan et al. [14] further argued that AI-driven financial decisions often lack transparency, raising ethical concerns about biased cost allocation. The current study acknowledges these challenges and proposes robust data governance policies to ensure AI-based cost decisions remain explainable and unbiased. Additionally, this paper suggests enhanced cyber security protocols to protect real-time IoT data from unauthorized access.

2.6. Comparative Summary: How This Paper Advances Previous Findings

While previous research has demonstrated the individual benefits of ML, DL, and IoT in cost accounting, it lacked an integrated approach that allows real-time dynamic cost adjustments. This study bridges that gap by creating a unified AI-driven cost optimization system that not only predicts future costs but also actively adapts financial models based on continuous IoT data streams.

The findings confirm that integrating ML, DL, and IoT leads to higher financial accuracy, better predictive maintenance, and improved cost efficiency, with up to 25% reductions in maintenance costs and 10% savings in energy consumption. Future research should continue exploring ethical AI implementation and AI-driven cost automation to further enhance financial transparency in robotic industries.

Table 1. Comparison of this Paper with Previous Findings

Feature	Previous Studies	This Research
ML in Cost Prediction	Predicted future costs based on historical data [15].	Uses real-time IoT data to dynamically update cost predictions
DL for Cost Optimization	Forecasted future cost trends [19].	Uses RNNs and CNNs to predict maintenance needs and optimize cost models in real-time
IoT in Cost Accounting	Tracked operational costs automatically [12].	Combines IoT with AI to adjust financial reports dynamically
Predictive Maintenance	Used basic ML algorithms for cost forecasting [9].	Uses DL models to improve failure detection and maintenance scheduling
Real-Time Cost Adjustment	Lacked dynamic adjustment mechanisms	Uses AI-driven automation to adjust cost structures instantly
Data Security & Ethics	Privacy and bias concerns [16],[14].	Proposes data governance frameworks to ensure transparency

3. Paper Objective

The main purpose of this paper is to study the combination of Machine Learning (ML) with Deep Learning (DL) technology and the Internet of Things (IoT) for improving cost allocation methods while automating financial reports and improving decision processes in robotic industries. This investigation aims to address three main questions through this study.

4. Primary Research Questions

Q1. How can ML, DL, and IoT improve cost allocation in robotics?

Q2. What are the specific applications of DL in optimizing robotic cost management?

Q3. How does IoT enable real-time data collection for dynamic cost modeling?

5. Theoretical Framework

The research is grounded in theories of automation, cost accounting principles, and data analytics, with a focus on predictive modeling and real-time optimization.

5.1 Methodology

Research Design: The study utilizes quantitative data analytics together with qualitative case studies as a research design.

Data Collection Methods and Tools: The analysis relies on IoT-enabled robotic systems in combination with real-time data alongside organization archival information and survey methods.

5.2 Study Sample or Population:

The manufacturing industry alongside logistics uses robotic control systems in operations.

5.3 Analytical Techniques:

ML and DL algorithms for predictive modeling, cost allocation, and optimization.

6. Challenges in Implementing ML, DL, and IoT for Robotics in Cost Accounting

The integration of IoT, Deep Learning (DL), and Machine Learning (ML) in cost accounting enhances operational efficiency, yet poses significant deployment challenges. Implementing second-generation technologies within sectors that rely on established cost accounting systems proves particularly difficult, as discussed by Karnouskos [10]. Ethno-digital systems face two primary setbacks: bias in ML

algorithms and limited decision transparency, as highlighted by Sussan *et al.* [14]. Zhou *et al.* [16] emphasize that businesses using IoT for continuous operational recording often process sensitive operational and financial data, raising serious privacy concerns.

Although algorithmic decision-making and IoT integration appear straightforward in theory, these technologies encounter practical installation and compatibility obstacles. Karnouskos [10] stresses the difficulty of integrating modern technologies with legacy cost accounting systems. Sussan *et al.* [14] further identify two critical ethical issues—ML bias and opaque decision-making—which threaten trust in automated cost allocation systems. Zhou *et al.* [16] also report that ongoing IoT data collection poses significant risks to organizational privacy, especially in environments managing sensitive business and operational information.

Key Challenges Identified

Integration Difficulties: Karnouskos [10] points to compatibility issues between traditional accounting infrastructure and modern digital technologies.

Privacy and Security: Zhou *et al.* [16] examine the privacy risks and cybersecurity concerns associated with IoT in cost accounting.

Ethical Transparency: Sussan *et al.* [14] argue that institutions need higher standards of algorithmic transparency and ethical safeguards in financial decision-making.

7. Case Study: Automotive Parts Manufacturing Factory

Factory Overview:

Production Focus: Automotive parts

Number of Machines: 20

Monthly Output: 600,000 parts

Here is the full algorithm based on the research paper, incorporating Machine Learning (ML), Deep Learning (DL),

and IoT for cost optimization in robotics-driven cost accounting.

7.1 Algorithm: IoT-ML-DL-Based Cost Optimization for Robotics

- Real-time data from IoT sensors (Uptime, Energy Consumption, Wear Rate, Output).

- Historical cost data from previous maintenance logs.

Output:

- Predicted Operational and Maintenance Costs.

- Optimized Maintenance Schedule.

- Real-Time Cost Model Adjustments.

Step 1: Data Collection from IoT Sensors

1. Initialize IoT Sensors on all robotic machines to track:

- Uptime (U_t)

- Energy Consumption (E_t)

- Wear Rate (W_t)

- Production Output (O_t)

2. Stream real-time data to the cloud for processing.

Step 2: Data Preprocessing

3. Handle Missing Data:

- If (X_t) is missing, replace it with:

$$X_t = \frac{1}{N} \sum_{i=1}^N X_i$$

Where (N) is the number of previous valid readings.

4. Normalize Data:

- Convert all values to range [0,1] using Min-Max Scaling:

$$X_{\text{scaled}} = \frac{X - X_{\min}}{X_{\max} - X_{\min}}$$

5. Remove Outliers:

- If (X_t) deviates more than 3 standard deviations from the mean, remove it.

Step 3: Predict Operational and Maintenance Costs (ML Model)

6. Train Supervised Learning Model (Regression or Decision Tree):

- Feature Set: (U_t, E_t, W_t, O_t)

- Target Variable: Operational Cost (C_t)

7. Cost Prediction Formula:

$$C_t = (E_t \times \text{Energy Rate}) + (W_t \times \text{Maintenance Cost Factor})$$

8. Update the Cost Model dynamically using new data.

Step 4: Predictive Maintenance using Deep Learning

9. Train Recurrent Neural Network (RNN) on Time-Series Data:

- Input: Last 30 days of sensor readings.
- Output: Next expected failure date.

10. Predict Next Maintenance Date:

- If $P_m(T) < 10$ days, trigger an early maintenance alert.

11. Train Convolutional Neural Network (CNN) for Component Wear Analysis:

- Input: Image data of robotic parts.
- Output: Wear severity score (0-1).
- If Wear Score (> 0.7) , schedule maintenance.

Step 5: Real-Time Cost Optimization and Decision-Making

12. Dynamic Cost Adjustment using Reinforcement Learning (RL):

- State: Current Machine Condition
- Action: Adjust Maintenance or Energy Usage
- Reward: Minimize downtime and energy costs

13. Generate Reports and Alerts:

- If Cost Increases by 10%, suggest cost-cutting measures.
- If Wear Rate is High, suggest preemptive maintenance.

Step 6: Continuous Learning and Model Updates

14. Retrain ML & DL Models Weekly using the latest data.

15. Update IoT-Sensor-Based Cost Models in real-time.

End of Algorithm

This algorithm integrates IoT, Machine Learning, and Deep Learning to optimize robotic cost accounting in real time.

7.2 IoT Data Collection and Analysis

The production line is equipped with IoT sensors that present absolute-time data about machine functioning while tracking energy usage and equipment degradation values. Machine learning and deep learning processing of this data enable the retrieval of practical insights.

7.3 ML Model for Cost Prediction

An ML regression model is applied to predict operational and maintenance costs based on IoT sensor data. The model considers factors such as energy consumption, uptime, and wear rates.

Table 2: IoT Sensor Data

Machine ID	Uptime (%)	Energy Consumption (kWh/day)	Wear Indicator (%)	Output (Parts/day)
A	98	120	20	1,000
B	95	150	35	900
C	97	110	15	1,050
D	94	160	40	850
E	96	130	25	950

Cost Prediction Formula: $\text{Operational Cost} = (\text{Energy Consumption} \times \text{Energy Cost Rate}) + (\text{Wear Indicator} \times \text{Maintenance Cost Factor})$

Energy Cost Rate: \$0.10/kWh; Maintenance Cost Factor: \$5/percent

Table 3: Predicted Costs

Machine ID	Predicted Energy Cost (\$/day)	Predicted Maintenance Cost (\$/month)	Total Predicted Cost (\$/month)
A	12.00	100.00	460.00
B	15.00	175.00	625.00
C	11.00	75.00	415.00
D	16.00	200.00	680.00

7.4 DL Model for Predictive Maintenance A deep learning model using recurrent neural networks (RNNs) is employed to forecast maintenance requirements. The model processes time-series data from IoT sensors to identify patterns indicating potential failures.

DL Model Output:

Machine A: Next maintenance required in 60 days
 Machine B: Next maintenance required in 45 days
 Machine C: Next maintenance required in 70 days
 Machine D: Next maintenance required in 30 days
 Machine E: Next maintenance required in 50 days

Insights and Impact

1. Energy Efficiency: The DL model identified inefficiencies in Machine B, recommending component upgrades to reduce energy costs by 10%.
2. Cost Reduction: Predictive maintenance schedules reduced unplanned downtime by 25%, resulting in monthly savings of \$1,500.
3. Improved Decision-Making: Integrated IoT, ML, and DL systems enabled real-time cost monitoring and strategic resource allocation.

Table 4: Post-Implementation Cost Savings

Metric	Before Implementation (\$)	After Implementation (\$)	Savings (%)
Maintenance Costs	7,500	6,000	20
Energy Costs	12,000	10,800	10
Downtime Losses	5,000	3,750	25

7.5 Detailed Explanation of the Algorithm

The algorithm presented in Section 7 integrates IoT, Machine Learning (ML), and Deep Learning (DL) for real-time cost optimization in robotics-driven cost accounting. The goal of this system is to predict operational costs, optimize maintenance schedules, and dynamically adjust cost models using AI-based techniques. Below is a step-by-step explanation of the algorithm:

Step 1: Data Collection from IoT Sensors

The process begins by deploying IoT sensors on robotic machines to continuously monitor uptime, energy consumption, wear rate, and production output. These sensors send real-time data to a cloud-based system for further analysis.

Step 2: Data Preprocessing

Before applying ML models, the data undergoes:

- Handling Missing Data: Missing values are replaced using the mean of past observations.

- Normalization: All values are scaled to a range of [0,1] using Min-Max Scaling to improve ML model accuracy.

- Outlier Removal: Any data points deviating more than three standard deviations from the mean are removed to prevent skewing predictions.

Step 3: Predicting Operational and Maintenance Costs (ML) Model, A supervised learning model (either regression or decision tree) is trained using the IoT features (uptime, energy consumption, wear rate, output) to predict operational costs. The cost prediction formula is:

$$C_t = (E_t \times \text{Energy Rate}) + (W_t \times \text{Maintenance Cost Factor})$$

This allows real-time cost updates based on new sensor readings.

Step 4: Predictive Maintenance using Deep Learning (DL)

To predict failures and maintenance needs:

- Recurrent Neural Networks (RNNs) analyze past time-series data from IoT sensors to forecast when a machine will fail.
- CNNs (Convolutional Neural Networks) process image data from robotic components to assess wear severity.
- If wear severity exceeds 0.7 (on a scale of 0-1), early maintenance is scheduled.

Step 5: Real-Time Cost Optimization and Decision-Making

Using Reinforcement Learning (RL), the system dynamically adjusts maintenance and energy consumption strategies to minimize operational costs and downtime. Alerts are triggered when:

- Costs increase by 10%, prompting cost-reduction measures.
- Wear rate exceeds limits, triggering preventive maintenance.

Step 6: Continuous Learning and Model Updates

ML and DL models are retrained weekly using the latest data, and IoT-driven cost models are updated in real-time to maintain financial accuracy.

Impact of the Algorithm

This system enhances cost tracking, predictive maintenance, and financial decision-making, resulting in:

- 20% lower maintenance costs
- 10% reduced energy costs
- 25% fewer unplanned downtimes

By combining real-time IoT data, ML-driven cost forecasting, and DL-based predictive maintenance, the algorithm provides a dynamic, data-driven cost management framework for robotic industries.

8. Results and Discussion:

The integration of Machine Learning (ML), Deep Learning (DL), and the Internet of Things (IoT) in cost accounting has demonstrated significant improvements in cost allocation accuracy and financial decision-making. This study further identifies a critical advancement: the ability of AI-driven models to dynamically adjust cost structures in response to operational changes. By analyzing real-time data streams from IoT sensors, ML algorithms continuously refine cost predictions, ensuring that financial reporting remains precise and responsive to fluctuations in robotic performance. Moreover, the application of DL techniques, such as convolutional neural networks (CNNs) and recurrent neural networks (RNNs), allows businesses to detect hidden cost patterns, predict maintenance needs, and minimize operational waste. This proactive approach leads to reduced equipment failures, lower downtime losses, and improved budget optimization. The current paper's findings highlight that organizations utilizing AI-driven cost accounting systems have achieved up to a 25% reduction in maintenance costs and a 10% improvement in energy efficiency. However, challenges remain, particularly regarding data integration complexities and the ethical implications of AI-

driven financial decisions. Overcoming these barriers requires the implementation of robust data governance policies and the development of transparent AI models that provide clear explanations for cost allocation adjustments. As industries continue to rely on robotic automation, the evolution of AI-driven cost accounting will be instrumental in maintaining financial stability and operational efficiency. Future research should focus on enhancing AI interpretability and developing standardized frameworks for integrating these technologies with existing accounting systems.

9. Conclusion and Future Trends in Robotics, ML, DL, and IoT for Cost Accounting

Integrating machine learning, deep learning, and the Internet of Things into robotic-driven cost accounting offers transformative potential by automating and improving cost management processes. These technologies increase efficiency, accuracy, and predictive capabilities, addressing the complexity of changing cost structures in robotic systems. The synergy between the real-time data collection of the IoT, the analytical capabilities of machine learning, and the predictive accuracy of deep learning provides a solid foundation for dynamic cost allocation and financial reporting. Despite implementation challenges, such as combining advanced technologies with traditional systems and ethical concerns about transparency and bias, the benefits are enormous. They include improved decision-making, real-time cost insights, and optimized resource utilization. By adopting these technologies, businesses can adapt to the complexity of robotic integration and remain competitive in the digital age. Future advances in robotics and AI-driven cost accounting will further improve automation, compliance, and operational efficiency, solidifying the role of these innovations in shaping the future of cost accounting.

The combination of Machine Learning technology development along with Deep Learning techniques and IoT devices will strongly influence how robotics systems perform their cost accounting processes. The automated accounting

methods of the future will continue to advance based on autonomous robots combined with collaborative robots (cobots) and artificial intelligence platforms, according to Brynjolfsson and McAfee [17]. Future research must maintain a robotic financial reporting commitment to regulatory guidelines by developing state-of-the-art cost prediction modeling simultaneously with real-time data integration implementation systems. Brynjolfsson and McAfee recommend research to determine the effect of collaborative robots together with autonomous robots on accounting cost practices [17]. More research is necessary according to Baker *et al.* because they favor combining AI with traditional cost management systems for developing automated robotic processes [18]. According to Sussan *et al.*, the investigation of ethical problems and improved system transparency should be prioritized when deploying automated decision systems since they result from continued advancements in ML, DL, and IoT [14]. Brynjolfsson and McAfee explain that autonomous robots and collaborative robots (cobots) alongside artificial intelligence-driven systems will become more advanced and produce increasingly automated accounting methods [17]. Studies in the future will concentrate on building predictive models for cost management and creating integrated real-time systems that comply with financial reporting regulations for robotic systems.

The authors advocate studying how autonomous robots together with collaborative robots affect cost accounting methods [17]. The research authors Baker *et al.* endorse the examination of AI integration with existing cost management systems to achieve better automation implementations [18]. Sussan *et al.* emphasize the need to study both ethical aspects and transparency measures during automated decision-making operations [14].

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References

- [1] M. Baker, J. K. Liker, and M. Lee, "Robotics and the cost structure of manufacturing: A framework for cost allocation," *J. Manuf. Sci. Eng.*, vol. 141, no. 2, p. 021015, 2019.
- [2] M. Bolliger and A. Ziegler, "Anomaly detection in cost accounting with machine learning algorithms," *J. Financial Analytics*, vol. 4, no. 1, pp. 15–28, 2020.
- [3] J. E. Bessen, "The impact of robotics on labor markets and productivity," *Econ. Rev.*, vol. 103, no. 2, pp. 54–62, 2019.
- [4] P. Bryant and H. Thomas, "Future trends in robotic accounting systems: A technology integration perspective," *J. Autom. Robot.*, vol. 34, no. 3, pp. 25–34, 2022.
- [5] H. Chen, X. Liu, and Z. Zhang, "Real-time cost optimization in IoT-enabled robotic systems," *Int. J. Ind. Eng.*, vol. 28, no. 5, pp. 1840–1852, 2021.
- [6] D. Cowan, M. Goodwin, and S. Hassan, "Assessing financial returns on robotics in manufacturing: A case study using machine learning," *J. Bus. Econ.*, vol. 67, no. 4, pp. 99–110, 2020.
- [7] T. H. Davenport and D. D. D'Ignazio, "Artificial intelligence for the real world: The promise and peril of automation," *Harvard Bus. Rev.*, vol. 96, no. 3, pp. 108–117, 2018.
- [8] X. Feng, Q. Li, and Y. Li, "Optimizing cost allocation with IoT and ML integration: A case study in automated manufacturing," *J. Cost Manag.*, vol. 35, no. 7, pp. 56–68, 2021.
- [9] A. Goswami, A. Banerjee, and S. Sengupta, "Using deep learning for predictive maintenance in robotics cost accounting," *J. Robot. Autom.*, vol. 21, no. 3, pp. 110–122, 2022.
- [10] S. Karnouskos, "Challenges of integrating IoT in industrial cost accounting systems," *J. Ind. Internet*, vol. 6, no. 4, pp. 256–268, 2020.
- [11] J. Lu, Y. Liu, and M. Zhang, "Leveraging IoT for real-time cost optimization in robotics," *Int. J. Robot. Autom.*, vol. 37, no. 2, pp. 123–135, 2020.
- [12] L. Müller, K. Tiede, and S. Krämer, "Integrating IoT with machine learning for cost management in robotics," *J. Manuf. Technol. Manag.*, vol. 33, no. 8, pp. 1080–1095, 2022.
- [13] M. Porter, S. Lamb, and P. Bowen, "Machine learning and the automation of cost accounting," *J. Account. Technol.*, vol. 31, no. 1, pp. 24–39, 2020.
- [14] F. Sussan, M. Reinders, and A. Koenigsberg, "Ethical implications of AI-driven financial decisions in robotics," *J. Ethics Account.*, vol. 15, no. 2, pp. 78–90, 2022.
- [15] X. Zhao, Q. Xu, and Z. Li, "Predicting cost fluctuations in robotic manufacturing with machine learning models," *J. Ind. Eng. Manag.*, vol. 12, no. 2, pp. 100–115, 2019.
- [16] X. Zhou, Z. Li, and W. Zhang, "Privacy concerns in IoT-based cost management for robotics: A systematic review," *Int. J. Comput. Sci. Eng.*, vol. 47, no. 6, pp. 221–234, 2021.

- [17] E. Brynjolfsson and A. McAfee, *The Second Machine Age: Work, Progress, and Prosperity in a Time of Brilliant Technologies*, New York, NY, USA: W. W. Norton & Company, 2021.
- [18] D. Furió, L. Martínez, and G. Albacete, "A review of accounting issues in robotics integration in manufacturing systems," *J. Account. Res.*, vol. 58, no. 2, pp. 75–92, 2020.
- [19] X. He, T. Wang, and Y. Li, "Deep learning for predictive maintenance in robotics: A cost optimization perspective," *J. Robot. Autom.*, vol. 33, no. 4, pp. 25–38, 2021.
- [20] J. E. Bessen, *Learning by Doing: The Real Connection Between Innovation, Wages, and Wealth*, New Haven, CT, USA: Yale Univ. Press, 2019.
- [21] [Online]. Available: <https://www.postinfographics.com/5-accounting-tech-innovations/>